



US009498759B2

(12) **United States Patent**
Griffiths et al.

(10) **Patent No.:** **US 9,498,759 B2**

(45) **Date of Patent:** ***Nov. 22, 2016**

(54) **COMPARTMENTALIZED SCREENING BY MICROFLUIDIC CONTROL**

(75) Inventors: **Andrew Griffiths**, Strasbourg (FR);
David Weitz, Cambridge, MA (US);
Keunho Ahn, San Diego, CA (US);
Darren R. Link, Lexington, MA (US);
Jerome Bibette, Paris (FR)

(73) Assignees: **President and Fellows of Harvard College**, Cambridge, MA (US); **Medical Research Council**, London (GB)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1272 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **11/665,145**

(22) PCT Filed: **Oct. 12, 2005**

(86) PCT No.: **PCT/GB2005/003924**

§ 371 (c)(1),

(2), (4) Date: **Sep. 8, 2008**

(87) PCT Pub. No.: **WO2006/040551**

PCT Pub. Date: **Apr. 20, 2006**

(65) **Prior Publication Data**

US 2009/0005254 A1 Jan. 1, 2009

Related U.S. Application Data

(63) Continuation of application No. 10/963,044, filed on Oct. 12, 2004, now abandoned.

(51) **Int. Cl.**

B01L 3/00 (2006.01)

B01F 5/06 (2006.01)

(Continued)

(52) **U.S. Cl.**

CPC **B01F 5/0646** (2013.01); **B01F 5/0256** (2013.01); **B01F 5/0647** (2013.01);

(Continued)

(58) **Field of Classification Search**

CPC B01F 13/0071; B01F 3/0807; B01F 5/0256;
C12Q 2563/159; C12Q 2565/119; B01L 3/502784; B01L 2200/0673; B01L 3/502761; B01L 2200/0652
USPC 506/2, 4, 79, 16, 18, 38
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,097,692 A 11/1937 Fiegel

2,164,172 A 6/1939 Dalton

(Continued)

FOREIGN PATENT DOCUMENTS

AU 2004225691 B2 6/2010

CA 2520548 A1 10/2004

(Continued)

OTHER PUBLICATIONS

Adang et al., "The Contribution of Combinatorial Chemistry to Lead Generation: An Interim Analysis", *Curr. Med. Chem.*, 8: 985-998 (2001).

(Continued)

Primary Examiner — Erik B Crawford

(74) *Attorney, Agent, or Firm* — Brown Rudnick LLP; Thomas C. Meyers

(57) **ABSTRACT**

The invention describes a method for the identification of compounds which bind to a target component of a biochemical system or modulate the activity of the target, comprising the steps of: a) compartmentalizing the compounds into microcapsules together with the target, such that only a subset of the repertoire is represented in multiple copies in any one microcapsule; and b) identifying the compound which binds to or modulates the activity of the target; wherein at least one step is performed under microfluidic control. The invention enables the screening of large repertoires of molecules which can serve as leads for drug development.

24 Claims, 27 Drawing Sheets

